Digestive disorders are increasingly common and affect millions of Americans. There were 41.3 million office visits to physicians and 15.1 visits to the emergency rooms for digestive-system symptoms in 2004, according to the Centers for Disease Control and Prevention’s (CDC’s) most recent data. Conditions include irritable bowel syndrome (IBS); inflammatory bowel diseases (IBDs), including ulcerative colitis and Crohn’s disease; celiac disease; gastroesophageal reflux disease (GERD); gastrointestinal (GI) cancers; and other conditions such as diarrhea, constipation, indigestion, nausea, and flatulence.

Approximately 60–70 million people are affected by overt diagnosable digestive diseases, yet tens of millions of other patients suffer from subclinical GI health conditions that alter their ability to absorb nutrients from their diets and supplements. This has a dramatic impact on quality of life with 1.9 million people disabled due to GI disease. Annually, an astounding 234,000 people die from GI diseases including GI cancer.

The GI tract is the absolute barrier between the burdensome outside world that enters the human body as foods and contaminants (herbicides, pesticides, heavy metals, and an array of other health saboteurs) and the well-ordered 75 trillion cells that work in harmony to sustain human existence. Therefore, regardless of whether an individual has any overt signs of GI dysfunction, fortifying the GI tract enhances the ability for nutrients from food and supplements to be most optimally absorbed.

**Intestinal Permeability and Overall Health**

Intestinal permeability, which refers to the potential for nutrients and bacteria to pass through a weakened intestinal wall—as well as, to some degree, through healthy tissues—is an important factor for optimal GI health. When intestinal permeability is increased, food and nutrient absorption is impaired. Dysfunctions in intestinal permeability can result in leaky gut syndrome, in which larger molecules in the intestines pass through them into the blood. This syndrome can trigger immediate damage and immune-system reactions because these large molecules are perceived as foreign. Progressive damage occurs to the intestinal lining, eventually allowing disease-causing bacteria, undigested food particles, and toxins to pass directly into the bloodstream.

Dysfunctions in intestinal permeability are associated not only with intestinal diseases, such as ulcerative colitis, IBS, and Crohn’s disease, but also with chronic fatigue syndrome, psoriasis, food allergies, autoimmune diseases, and arthritis. Impaired intestinal permeability can also occur in patients undergoing chemotherapy and patients with heart disease, such as those with chronic heart failure. A dysfunction in intestinal permeability may be present when an individual is consuming a less-than-optimal diet or as the result of other factors such as psychologic stress.

Intestinal permeability is associated with food sensitivity. One group of researchers evaluated the intestinal permeability of subjects with adverse reactions to food. Twenty-one subjects with food allergy and 20 with food hypersensitivity who were on allergen-free diets were enrolled in the study and divided into 4 groups according to the seriousness of their clinical symptoms. The researchers found statistically significant differences in intestinal permeability in subjects with food allergy or hypersensitivity compared with control patients. The results showed that the worse the intestinal permeability was, the more serious were the clinical symptoms in patients with food allergy and hypersensitivity.

Impaired intestinal permeability is often linked with GI diseases such as ulcerative colitis and Crohn’s disease. However,
new research is finding a surprising link between malfunctions in the colonic barrier and a number of non-GI conditions such as heart disease. In a recent study, scientists evaluated the function of the gut in 22 patients with chronic heart failure (CHF) and 22 control subjects. Patients with CHF, compared with control patients, had a 35% increase of small-intestinal permeability and a 210% increase of large-intestinal permeability. In addition, higher concentrations of adherent bacteria were found within the mucus of patients who had CHF compared with control subjects. The researchers suggested that CHF is a disorder in which intestinal morphology, permeability, and absorption are altered and may contribute to the origin of both chronic inflammation and malnutrition in this condition.7

The Role of Short-Chain Fatty Acids

Short-chain fatty acids (SCFAs), primarily acetate, propionate, and butyrate, are produced in the colon by fermentation of dietary carbohydrates, particularly from degradation-resistant starches and dietary fiber. These fatty acids play an important role in intestinal health. The amount and rate of SCFA production depends on several factors. These include the species and amounts of microflora in the colon, the fermentation substrate source, and the transit time of fecal matter through the gut. SCFA concentrations in the intestines vary markedly with diet.8

SCFAs have numerous functions in the intestines. SCFAs are readily absorbed by the intestinal mucosa and have been shown to stimulate intestinal mucosal growth. In particular, butyrate is the major energy source for the cells that line the colon. Butyrate has been shown to induce enzymes promoting mucosal-cell restoration.

SCFAs also stimulate sodium and water absorption in the colon.9 In addition, SCFAs enhance the motility of the intestinal tract by stimulating contractions and shortening of ileum emptying, which may protect ileal mucosa against the potentially harmful effects of reflux of colonic contents.10 In addition, mucus secretion, an important part of the intestinal mucosal barrier, has been shown to be stimulated by SCFAs, especially butyrate, in the colon.11

SCFAs have been shown to play a role in many disease conditions, including cancer, cardiovascular disease, and digestive disorders.12 Propionate has been shown to inhibit cholesterol synthesis, making it an important factor in cardiovascular disease.13

Butyrate, acetate, and propionate have been shown to be effective anti-inflammatory and immune-modulating agents in human colon-cancer cell lines and mouse models.14 Butyrate, propionate, and acetate inhibited the proliferation and migration and increased the differentiation of a human colon-cancer cell line in studies.15 In particular, butyrate has been investigated for its inhibition of proinflammatory markers and the role this plays in prevention of IBD and colon cancer.16 Butyrate has also been studied in the prevention of colon cancer, by promoting cell differentiation, cell-cycle arrest, and apoptosis of transformed colon cells. Butyrate has also been shown to decrease experimentally induced DNA damage in human colon cells and colon-cancer cell lines by approximately 50%.17

Butyrate may also play a role in preventing certain types of colitis. A deficiency of SCFAs could lead, in the short-term, to incomplete development of the mucosal lining and, in the long-term, to colitis.18 Some researchers believe that a diet low in resistant starch and fiber and the resulting low production of SCFAs in the colon, may explain the high occurrence of colon disorders seen in Western societies.19 Decreased production of SCFAs appears to be involved in antibiotic-associated diarrhea, diversion colitis,* and possibly in pouchitis.† SCFA deficiency also may play a role in the development of ulcerative colitis and other intestinal disorders.20 Thus, SCFAs may reduce the risk of developing cancer, GI disorders, and cardiovascular disease.22

Nutritional Support for Optimal Colon Health

Glutamine
Glycyrrhiza glabra (licorice)
Berberine Hydrastis canadensis (goldenseal) and Mahonia aquifolium (Oregon grape)
Brassica oleracea (cabbage)
Ulmus fulva (slippery elm)
Althaea officinalis (marshmallow)
Aloe vera (aloe)
N-acetyl-glucosamine
Phosphatidylcholine
Gamma-oryzanol
Fiber
Larch arabinogalactan
Probiotics
Vitamin D3
Short-chain fatty acids

SCFAs may reduce the risk of developing cancer, GI disorders, and cardiovascular disease.

*This inflammation develops in a lower part of the large intestine after the passage of stool above this intestine has been surgically diverted.
†This inflammation of a surgically made pouch from the ileum can occur in patients who undergo restorative proctocolectomy.
Glutamine is one of the most powerful tools for reducing intestinal permeability, thereby protecting the body against the negative consequences of a leaky gut. In a recent review, researchers studied the medical literature to determine if glutamine was effective in reducing intestinal permeability in critically ill patients. In this patient population, intestinal permeability can have particularly lethal consequences, causing bacteremia, sepsis, and multiple organ failure syndrome. The scientists concluded that glutamine has a protective effect that prevents or reduces increases in intestinal permeability. Glutamine also reduces the frequency of systemic infections.

Another group of researchers drew a similar conclusion after studying patients with GI cancer who received chemotherapy. In these subjects, oral glutamine decreased intestinal permeability and maintained the intestinal barrier. Studies using animal models also suggest that, in addition to improving intestinal permeability and decreasing bacterial translocation, glutamine supplementation may also decrease systemic inflammation and increase killing of bacteria by the immune system.

Licorice

*Glycyrrhiza glabra* (licorice) has historically been used for its anti-inflammatory, soothing, laxative, and antispasmodic activities. Most of the research on deglycyrrhizinated licorice (DGL) has been focused on upper GI health, including ulcer healing and dyspepsia. DGL seems to have similar properties as carbamazepine, a semisynthetic derivative of glycyrrhetic acid used outside the United States for treating gastric and duodenal ulcer disease. DGL utility is not limited to upper GI health, as in the clinical setting DGL has also demonstrated great utility in lessening intestinal irritation and related symptoms.

Berberine

Berberine is a constituent found in multiple herbs such as *Hydrastis canadensis* (goldenseal) and *Mahonia aquafolium* (Oregon grape). Berberine may benefit colon health by maintaining healthy GI flora and inhibiting pathogenic microbes in the colon. Berberine has antimicrobial effects, including antibacterial, antifungal, antimycobacterial, and antiprotozoal activity.

Based on animal models, berberine may reduce intestinal permeability. Research has also shown that berberine induces apoptosis in human colon-cancer cells. In addition, berberine has decreased inflammation in experimentally induced colitis in rats by decreasing the cytokine interleukin (IL)–8, which is commonly elevated in individuals with ulcerative colitis and Crohn’s disease.

Dietary and Herbal Support for the Colon

Specific supplements, taken together, can provide critical building blocks for daily repair of the GI tract and also help soothe irritation that arises from innate colonic function.

Glutamine

Glutamine is the most-abundant free amino acid in the body. Though this substance is classified as a nonessential amino acid, it is a conditionally essential amino acid during times of increased stress. Glutamine serves as metabolic fuel for the enterocytes that line the colon and the small intestine and that may play a role in cell proliferation and differentiation. The GI tract has the largest demand for glutamine in the body. Insufficient glutamine can cause atrophy, ulceration, and necrosis of the colon lining.

Adverse Effects of Ammonia in the Colon

Ammonia is produced in the colon as a byproduct of bacterial fermentation of protein and other nitrogen-containing substances. Levels of ammonia in the colon increase as protein intake increases. Elevated levels of colonic ammonia may have adverse health effects. Research indicates that ammonia levels as low as 5 mmol/L can have detrimental effects on the epithelial cells that line the colon. The toxicity of ammonia in colonic epithelial cells can lead to cell destruction and increased turnover of these cells. In addition, increased production of ammonia from eating a high-protein diet was shown to increase the incidence of colon cancer in animal models. Levels of ammonia found in the colons of individuals consuming a typical Western diet were associated with increased viral infections, promotion of growth of cancer cells, cell toxicity and altered nucleic-acid synthesis, and increased mass of intestinal mucosal cells.
Cabbage

Brassica oleracea (cabbage) constituents offer significant protection to the GI tract. Cabbage contains several important nutrients, such as vitamins A, B (such as folic acid), C, E, and K1; calcium; and amino acids including glutamine. Evidence suggests that individuals who consume large amounts of cabbage and other Brassica vegetables have a lower risk of developing stomach and colorectal cancer.44

In a study, 100 patients who had peptic ulcers drank 4 glasses of fresh, raw cabbage juice daily. The patients reported having dramatically reduced pain, while X-rays showed significantly reduced healing time. Eighty-one percent of the patients were symptom-free within 1 week, and more than two thirds were better within 4 days.45 Cabbage also produces antioxidant activity.46

Slippery Elm

The inner bark of Ulmus fulva (slippery elm) contains mucilage constituents that are demulcent and emollient. Slippery-elm preparations trigger gentle stimulation of nerve endings in the GI tract, leading to mucus secretion that coats and protects the delicate lining of the intestines from ulcers, excess acidity, ingested irritants, and toxins.47 In addition, a study evaluated damaging oxygen-free radical release from mucosal biopsies from patients with active ulcerative colitis. Incubation with slippery elm reduced oxygen-free radicals showing antioxidant activity in the colon.48

Marshmallow

Althaea officinalis (marshmallow) leaf and root contain mucilage polysaccharides that soothe and protect mucous membranes by creating a protective layer against local irritants.49,50 These mucilage constituents can also have antimicrobial, spasmylytic, and wound-healing effects.49,51

Aloe

Aloe vera (aloe) is commonly used for digestive problems, such as constipation, IBD, and ulcers. Research has demonstrated that aloe gel has antioxidant and anti-inflammatory activity in the colon, and decreases levels of colorectal prostaglandin E2 and IL-8, which have been shown to play a role in inflammatory bowel disease.52

In a double-blind, randomized, placebo-controlled study, aloe gel was administered at a dose of 100 mL, twice daily, for 4 weeks to patients with mild-to-moderate active ulcerative colitis. At the end of the study, 30% of patients had clinical remissions, improvement was seen in 37%, and 47% responded to treatment. Simple Clinical Colitis Activity Index and histologic scores decreased significantly during treatment as well.53 Aloe gel also has antibacterial and antifungal activity.54

N-Acetyl-Glucosamine

N-acetyl-glucosamine (NAG) is the acetylated derivative of the amino sugar glucosamine. NAG, a precursor to proteoglycans, is a major constituent of the mucosal barrier covering absorptive enterocytes and protects these cells from the damaging effects of digestive enzymes. Studies indicate that, in individuals with IBD, N-acetylation of glucosamine is relatively deficient in the intestinal mucosa, possibly reducing the synthesis of the gastric and intestinal mucosa’s protective glycoprotein cover.55

Phosphatidylcholine

Phosphatidylcholine is an important lipid component of the protective intestinal mucosal layer. A defective phosphatidylcholine layer may contribute to increased inflammation and ulceration. Animal models suggest that treatment with lipids, including phosphatidylcholine, increases surface hydrophobicity in the colon and reduces colonic permeability.56 This surface hydrophobicity is an important defense mechanism against macromolecules and toxins.

Low levels of phosphatidylcholine in colonic mucus are a likely contributory factor in the development of ulcerative colitis. In a recent, randomized, double-blind placebo-controlled study, patients with ulcerative colitis were given 2 g per day of phosphatidylcholine. Phosphatidylcholine supplementation reduced corticosteroid dependence in patients with chronic steroid-refractory ulcerative colitis.57

In a similar study, 6 g per day of phosphatidylcholine (using delayed- or “retarded-” release phosphatidylcholine) was administered to patients with ulcerative colitis over 3 months.58 At the end of the study, 53% of patients had clinical remission, while 90% had improvement. In addition, 55% of the patients treated with phosphatidylcholine reported improvements in quality of life, 63% had reductions in length of affected areas, and 52% had improvement in histology scores as noted by evaluation.58

Research also suggests that phosphatidylcholine can enhance butyrate’s ability to inhibit colon-cancer cells, and, therefore works well with fiber to strengthen the intestinal environment.59
Larch arabinogalactan (AG) is a highly-branched polysaccharide derived from the bark of the Larix spp. (larch) tree, primarily L. occidentalis (Western larch). AG, which is approved by the Food and Drug Administration as a dietary fiber source, is a nondigestible, soluble dietary fiber that resists breakdown by enzymes and enters the large bowel intact, where this fiber is fermented by colonic bacteria. Larch AG is used medicinally for the effects of these polysaccharides on the intestines and immune system.

Larch AG has been shown to increase the production of short-chain fatty acids, particularly butyrate and propionate. This fiber has decreased the generation and absorption of ammonia in the colon. In addition, research has demonstrated that ingestion of Larch AG has a significant effect on enhancing beneficial gut microflora, specifically increasing anaerobes such as Lactobacillus.

To assess the effects of Larch AG on healthy individuals, participants in a study were given either 15 or 30 g of Larch AG daily for 6 weeks. Ingestion of Larch AG increased levels of the total anaerobic bacteria in the colon and significantly increased Lactobacillus levels. Fecal ammonia levels also decreased significantly, which may have been the result of the increase in anaerobic bacteria, because some strains use ammonia as a preferred nitrogen source.

Larch AG also has immune-modulating activity, which is important for several intestinal disorders. This substance has stimulated natural-killer (NK) cell cytotoxicity, which can be abnormal in conditions such as IBS and IBD. Larch AG also can inhibit metastasis of tumor cells to the liver, making this substance an important adjunct to cancer protocols.

Probiotics

There are more than 400 different strains of bacteria in the intestines. Proper intestinal microflora are necessary for optimal health and are critical for normal immune system functioning. For example, in many studies, probiotics, such as Lactobacillus and Bifidobacteria, have provided health benefits. Probiotics can improve the barrier function of the intestines, compete with and suppress pathogenic bacteria, and modulate or stimulate the immune response.

A recent study showed that giving probiotics and prebiotics to patients with colon cancer decreased cell proliferation and other cancer markers while stimulating the immune response. In addition, taking supplements with these beneficial bacteria decreased the levels of pathogenic bacteria in the colon.

Taking Lactobacillus to increase colonic levels of this organism has shown benefit for patients with several intestinal disorders including diarrhea, chronic IBD, ulcerative colitis, IBS, and pouchitis.

Vitamin D

Vitamin D has been shown to play an important role in GI health. Evidence suggests that, in patients with IBD, vitamin D deficiency (a serum 25OHD$_3$ concentration of less than 15 ng/mL) is present in 22–70% in patients with Crohn’s disease and in 45% of those with ulcerative colitis.

Animal models suggest that the vitamin D receptor is involved in mucosal-barrier homeostasis by preserving the integrity of tight-junction complexes and the healing capacity.
of the colon epithelium. Tight junctions are intercellular junctions that provide a functional barrier and regulate paracellular permeability across the epithelium. This evidence suggests that vitamin D deficiency may compromise the mucosal barrier, leading to increased susceptibility to mucosal damage and increased risk of IBD.70

Vitamin D deficiency has also been shown to play a role in cancer development. Studies indicate an inverse relationship between vitamin D intake and colon cancer. There appears to be a dose–response relationship between vitamin D intake and serum 25OHD3 and risk for colon cancer. Observational studies have shown that individuals with a >1000 international units (IU) per day oral vitamin D intake had 50% lower risk for developing colon cancer.71 In addition, vitamin D3 metabolites have recently been shown to play an important role in the regulation of cellular proliferation, differentiation, and apoptosis.72

**Conclusion**

Digestive disorders are increasingly common. Optimal colon health is paramount in effectively managing patients with these conditions. Several nutritional supplements, herbs, and foods may help provide substantial improvement in GI function and GI-related symptoms.

**References**

37. Rehman J, Dillow JM, Carter SM, et al. Increased production of antigen-specific 
immunoglobulins G and M following in vivo treatment with the 
38. Sun D, Courtney HS, Beachey EH. Berberine sulfate blocks adherence of 
Streptococcus pyogenes to epithelial cells, fibronectin, and hexadecane. Antiimi-
on the growth and structure of Entamoeba histolytica. Giardia lamblia and 
40. Fukuda K, Hibiya Y, Mutoh M, et al. Inhibition by berberine of cyclooxy-
genase-2 transcriptional activity in human colon cancer cells. J Ethnopharma-
41. Taylor CT, Winter DC, Skelly MM, et al. Berberine inhibits ion transport 
human colonic carcinoma cells through generation of reactive oxygen species 
and activation of JNK/p38 MAPK and FasL. Arch Toxicol 2007;81:719–728.
43. Zhou H, Mineshita S. The effect of berberine chloride on experimental 
44. van Poppeg V, Verhoeven DT, Verhagen H, et al. Brassica vegetables 
1999;472:159–168.
45. Cheney G. Vitamin U Therapy of Peptic Ulcer. California Med 1952;77: 
248–252.
46. Ishib T, Yslin I, Ayin M, et al. The effects of Brassica oleracea var capitata 
on epidermal glutathione and lipid peroxides in DMBA-initiated-TPA-
47. The Review of Natural Products by Facts and Comparisons. St. Louis: 
therapy used by patients with inflammatory bowel disease: An in vitro study. 
Mary Ann Liebert, Inc., 1999.
53. Burton AF, Anderson FH. Decreased incorporation of 14C-glucosamine 
relative to 3H-N-acetyl glucosamine in the intestinal mucosa of patients with 
54. Lugea A, Salas A, CASALO J, et al. Surface hydropathy of the rat 
colonic mucosa is a defensive barrier against macromolecules and toxins. Gut 
steroid-refractory chronic ulcerative colitis: A randomized trial. Ann Intern 
fatty acid–enriched phosphatidylcholine and phosphatidyserine on butyrate-
induced growth inhibition, differentiation and apoptosis in Caco-2 cells. Cell 
Biochem Funct 2006;24:159–165.
59. Cicero AF, Gaddi A. Rice bran oil and gamma-oryzanol in the treat-
ment of hyperlipoproteinemas and other conditions. Phytotherapy Res 2001; 
15:277–289.
60. Seetharamaiah GS, Chandrasekhar N. Effect of oryzanol on cholesterol 
on inflammatory bowel disease and colon cancer: Importance of fermentation 
62. Kelly GS. Larch arabinogalactan: Clinical relevance of a novel immune-
63. Fedorak RN, Madsen KL. Probiotics and the management of inflamma-
risk factors in polypectomized and colon cancer patients. Am J Clin Nutr 
2007;85:488–496.
flora is associated with reduction in abdominal bloating and pain in patients 
67. Pappa HM, Grand RJ, Gordon CM. Report on the vitamin D status of 
adult and pediatric patients with inflammatory bowel disease and its signifi-
in maintaining the integrity of the intestinal mucosal barrier. Am J Physiol 
Gastrointest Liver Physiol 2008;294:G208–G216.
70. Kim KE, Brasitus TA. The role of vitamin D in normal and pathologic 

Chris D. Meletis, N.D., is executive director of the Institute for Healthy Ag-
ing, a non-profit educational group, in Carson City, Nevada, and an associate 
professor of natural pharmacology at the National College of Natural Medi-
cine, in Portland, Oregon. Nieske Zabriskie, N.D., is a naturopathic doctor in 
Grand Rapids, Michigan.

To order reprints of this article, e-mail Karen Ballen at: Kballen@liebertpub.com or call at (914) 740-2100.